The anaerobe faecal flora and their fermentation products in health and disease

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CHAPTER VII

Summary and discussion

The indigenous microflora in man is a complex ecosystem, which can be characterised in several ways. The conventional approach is that of qualitatively and quantitatively culturing the faecal anaerobes, being numerically the most important component (99.9%) [Chapter I]. New techniques for characterisation of the intestinal flora, should however be developed. Obviously these should correlate significantly with the "golden standard" to be considered for replacement of this time-consuming conventional culturing technique. We investigated the anaerobe faecal flora of ten healthy human volunteers over a one year period to provide insight into the stability and the comparability of different flora [Chapter II]. Since we found the colony counts of anaerobes comparable with the direct microscopic clump counts and thus reliable, a basis was obtained for further studies with antibiotics and their effects on the anaerobe faecal flora of healthy controls and (immunocompromised) patients.

Antimicrobial agents that have minimal ecological impact on the intestinal microflora should preferentially be used in (neutropenic) patients. These agents have to be completely absorbed after oral administration as well as following biliary excretion, when administered parenterally.

Norfloxacin or trimethoprim/sulfamethoxazole, both in combination with amphotericin-B, were given to neutropenic patients for infection profylaxis by selective decontamination (SD) in a prospective randomised trial [Chapter III]. Two indices of an impaired colonisation resistance were used in this study: ≥ 3 log increase or decrease in counts of faecal anaerobes, and the appearance of *Clostridium difficile* or yeasts during treatment with antimicrobial agents and/or antineoplastic agents. For infection prophylaxis by SD, norfloxacin was found to be the best choice in a daily oral dosage of 1200 mg plus 37.5 mg amphotericin-B.

Searching for a more solid basis for the conclusion that determination of SCFA and organic acid concentrations cannot replace anaerobe cultural counts in faecal flora studies with healthy human volunteers, a long term study in 10 healthy volunteers was performed. Faecal cultural counts were determined simultaneously with the faecal concentrations of SCFA and organic acids [Chapter IV]. Only 4.7% significant correlations were found between these faecal flora variables. This means that we could not establish the relation between faecal SCFA/organic acid concentrations and faecal cultural counts in this group of volunteers.

In a study with healthy volunteers, during administration of the broad-spectrum antibiotic ceftriaxone, we found the significantly decreased propionic acid concentrations to have a predictive value for a significant decrease in bacteroides cultural counts [Chapter

V]. These faecal flora variables correlated very well (r = 0.94). Most SCFA significantly decreased and lactic acid concentrations significantly increased. Certain SCFA concentrations could probably be used as a predictor of faecal flora disturbances when the cultural counts of the intestinal flora are significantly decreased by antibiotic administration. To test this hypothesis we applied the same techniques to the faecal flora of patients receiving FCE 22891, a new oral carbapenem, for acute infectious complications of their chronic obstructive pulmonary disease [Chapter VI]. None of the significantly changed SCFA and organic acid concentrations in this study correlated with the significantly increased bacteroides colony counts at the end of therapy and, therefore, had no predictive value. Lactic acid concentrations were also significantly increased during this treatment, reflecting a lower bacterial metabolism. When the SCFA and organic acid concentrations of the patients were compared to those of untreated healthy volunteers, more and other significant decreases were found during, and also after treatment. The colony counts of the *Bacteroides* species were significantly lower and those of the anaerobes growing on *C. difficile* agar were significantly higher, than those of the healthy controls in the study period. This means that samples from patients during treatment should not only be compared to their own controls (baseline sample before treatment), but also to those of healthy controls.

When antibiotics are investigated for their influence on the faecal flora, the MIC values of the faecal isolates compared to the biologically active concentration of the drug in faeces, provide insight into the effect of drugs on the colony counts of different groups of bacteria in faeces.

It can be concluded from our study that SCFA concentrations and probably also organic acid concentrations can be used to rapidly characterise the faecal flora of an individual only when a serious disturbance has been caused by antimicrobial or antineoplastic agents. In general, determination of SCFA concentrations cannot replace colony counts in normal flora studies and should, therefore, be performed simultaneously to provide extra information about the effect of drugs on the faecal flora.